Remarks

Reconsideration of this Application is respectfully requested.

Claims 40-45 and 47-57 are pending in the application, with claim 40 being the sole independent claim.

I. Claim Rejections Under 35 U.S.C. § 103

A. Kim in View of Wang and Woodfield

Claims 40-45 and 47-56 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kim *et al.*, *Genome Res. 8*:404-412 (1998) ("Kim") in view of Wang *et al.*, *J. Virol. 70*:8422-8430 (1996) ("Wang") as evidenced by Woodfield *et al.*, *Nucl. Acids. Res. 28*:3323-3331 (2000) ("Woodfield"). *See* Office Action, page 2. Applicants respectfully traverse this rejection for the reasons set forth in Applicants' Amendment and Reply filed on January 4, 2006, and provide the following additional remarks.

The currently pending claims are directed to methods for converting a large capacity cloning vector (*e.g.*, a BAC) into a herpes simplex virus (HSV)-based amplicon. The methods comprise recombining: (a) a large capacity cloning vector comprising a genomic DNA insert; and (b) an amplicon vector comprising a herpesvirus cleavage/packaging sequence and a herpesvirus origin of replication.

As noted in Applicants' previous response, Kim refers to recombining a BAC clone with a DNA construct containing the GFP reporter gene and the *neo* selectable marker gene

in order to introduce the GFP and *neo* genes into the BAC. *See* Kim, page 405, left column, and page 406, Figure 1. Wang refers to hybrid "miniviral vectors" (amplicons) that contain an HSV-1 origin of DNA replication and an HSV-1 viral packaging sequence as well as the *lacZ* reporter gene. *See* Wang, page 8424, paragraph bridging left and right columns, and Figure 1. Neither reference, however, teaches or suggests recombining a BAC and an amplicon vector.

The Examiner, however, has maintained the rejection based on the argument that a person of ordinary skill in the art would have been motivated to combine the "teachings" of Kim and Wang. According to the Examiner, a person of ordinary skill in the art would have been motivated to combine these references because of the supposed advantages associated with the vectors of Wang that would have allegedly been recognized by a person of ordinary skill in the art. As asserted by the Examiner:

> When the teachings of Kim *et al.* and Wang *et al.* are viewed as a whole, the skilled artisan would clearly perceive an advantage in using the amplicon vector of Wang *et al.*, which would allow the skilled artisan to obtain a large number of mammalian cells comprising BAC clones without the need for antibiotic selection, as compared with the relatively inefficient method of transfection using BAC vectors retrofit with only selectable markers as taught by Kim *et al.*

See Office Action, sentence bridging pages 4-5.

In other words, according to the Examiner, a person of ordinary skill in the art would have been motivated to combine the references in order to improve the efficiency with which BAC clones are introduced into mammalian cells without the need for antibiotic selection. Applicants do not agree that a skilled person would have been so motivated; however, even

if such a motivation did exist, a person of ordinary skill in the art, in view of Kim and Wang, could have achieved the alleged improved efficiencies without recombining a BAC with an amplicon vector.

If the Examiner is correct that "[w]hen the teachings of Kim *et al.* and Wang *et al.* are viewed as a whole, the skilled artisan would clearly perceive an advantage in using the amplicon vector of Wang *et al.*," it logically follows that the skilled artisan would have simply inserted the genomic insert of Kim (containing the GFP, *neo* and *lacZ* genes) into the amplicon vector of Wang using the same standard molecular cloning techniques that were used by Wang to create the amplicon vector set forth therein (*i.e.*, pH300-lac). According to Wang, "pH300-lac was constructed by inserting a *lacZ* gene into the *Hin*dIII and *Not*I sites of the multiple cloning site of pH300." If the Examiner's reasoning is followed, a person of ordinary skill in the art who was interested in improving the delivery efficiency of the genomic insert of Kim into mammalian cells using the amplicon vector of Wang would have simply inserted the genomic insert of Kim into the multiple cloning site of the Wang vector using standard restriction enzyme and ligation reactions. Such a process would be outside the scope of the currently presented claims.

Stated differently, the result that the Examiner asserts a person of ordinary skill in the art would have been motivated to achieve -- *i.e.*, improving the efficiency of genomic insert delivery into cells without the use of antibiotic selection -- could have been achieved by simply cloning the genomic insert into the amplicon vector. There is nothing in either Kim or Wang that would have suggested *recombining* the entire BAC of Kim with the amplicon of Wang.

Kim uses recombination to insert the GFP and *neo* genes into a BAC clone. Nonetheless, there would have been no reason for a person of ordinary skill in the art to use *recombination* to take advantage of the features of the Wang amplicon. In fact, having already subjected the BAC of Kim to one round of recombination, a person of ordinary skill in the art would have been precluded from subjecting the resulting "retrofitted BAC clone" to *another* round of recombination since there would be no available recombination sites. *See* Kim, page 406, Fig. 1. In addition, the amplicon of Wang lacks a recombination site. Thus, simply combining the "teachings" of Kim and Wang would not result in a process that falls within the scope of the currently pending claims.

In summary, the only recombination reaction mentioned in either Kim or Wang involves the insertion of a genomic DNA insert into a BAC clone, as shown in Kim. There is no suggestion that the end product of this recombination (*i.e.*, the "retrofitted BAC clone" of Kim) should, or even could, be further recombined with the amplicon vector of Wang. The advantages that would have allegedly been recognized by a person of ordinary skill in the art after reading Kim and Wang could have readily been achieved through simple DNA cloning techniques (as illustrated in Wang) without any reason to include an *additional* recombination step. Thus, even if a person of ordinary skill in the art were motivated in the manner suggested by the Examiner, such motivation would not have resulted in the practice of a method that falls within the scope of the currently presented claims. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

B. Kim in View of Wang and Saeki

Claims 40, 56 and 57 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kim in view of Wang and further in view of Saeki *et al.*, *Hum. Gene Ther. 9*:2787-2794 (1998). *See* Office Action, page 3. Applicants respectfully traverse this rejection.

The rationale for this rejection assumes that the subject matter of claims 40 and 56 would have been obvious in view of Kim and Wang. *See* Office Action dated August 9, 2005, page 12. As explained above and in Applicants' previous response, the subject matter of claims 40 and 56 would *not* have been obvious in view of Kim and Wang. Thus, for at least the reasons set forth above, Applicants submit that the obviousness rejection of claims 40, 56 and 57 based on Kim, Wang and Saeki is improper. Applicants respectfully request that this rejection be reconsidered and withdrawn

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and that, as such, the present application is in condition for immediate allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,
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